## REMARKS

Claims 1 – 3 are pending in this application. Claims 1 – 2 are amended without prejudice. Support for the amendments can be found in the original claims and the abstract. Applicants submit that no new matter is introduced into the application by these amendments.

***Claim Rejections - 35 USC §112, first paragraph – enablement.***

The Examiner rejects claims 1 to 3 under 35 U.S.C. §112, first paragraph as not being enabled in the specification. The Examiner points out that the solvents N,N-dimethylformamide,dimethoxymethane, 2,2-dimethoxypropane, and 1,2-dimethoxyethane are described while claim 1 recites "dimethylacetyls of lower aliphatic aldehydes, dimethyketals of lower aliphatic ketones and 1,2-dialkoxyethane." On this basis, the Examiner states that the claims are not enabled across their full scope.

The Examiner refers to *In re Wands* where factors that are to be considered for determining enablement are discussed. The Examiner points out the factors as the breadth of the claims, nature of the invention, state-of prior art, amount of direction provided by the inventors/working examples, and quantity of experimentation needed.

As to the nature of the invention, the examiner states that all acetals and ketals are within the claim scope since lower aliphatic is not defined in the specification. The skilled artisan knows that lower aliphatic aldehyde refers to 1 to 4 carbon groups and a specification need not describe that which is conventional. Moreover, all acetals or ketals are not the end but only dimethyl acetals or dimethyl ketals of lower aliphatic aldehydes or ketones, respectively. Indeed, the present application describes the solvents:

> [0072] Various solvents, a list of which is given hereinbelow were tried for crystallization of perindopril erbumine, manufactured by any of the prior art methods or through methods invented by the inventors. These solvents are:
>
> [0073] a) Ethers, both cyclic and acyclic, such as tetrahydrofuran, diethyl ether, diisopropyl ether etc.;
>
> [0074] b) Ketonic solvents, both cyclic and acyclic, such as acetone, methyl ethyl ketone, methyl isobutyl ketone, 2-pentanone, cyclopentanone, cyclopentanone etc.;
>
> [0075] c) Hydrocarbons, both aliphatic and aromatic, such as n-hexane, n-heptane, toluene, chlorobenzene etc;
>
> [0076] d) Nitroalkanes, such as nitromethane, nitroethane, nitropropane etc.
>
> [0077] However, all the solvents were found to give either the .alpha.- or .beta.-crystalline forms exclusively.
>
> [0078] Against this backdrop, the applicants have found that solvents selected from N,N-dimethylformamide or dimethyl acetals of lower aliphatic aldehydes and ketones give exclusively the crystalline form of perindopril erbumine having identical and/or superimposable IR

> spectrum, DSC thermogram and X-ray (powder) diffraction pattern to that obtained on crystallization of perindopril erbumine from ethyl acetate as per the method described in Example Stage 3D, column 9 of U.S. Pat. No. 4,914,214.
>
> [0079] These solvents, unlike those used in the prior art, such as acetonitrile, 1,4-dioxane, dichloromethane, chloroform etc. are tolerated better by International Conference on Harmonization (ICH), and thereby rendering the process more amenable for commercial manufacture from a safety, environmental and regulatory point of view.

See U.S. pre-grant publication 2007/0149604. Against this backdrop, the skilled artisan would readily appreciate the genus of solvents recited in claim 1.

As to the state-of art or level of predictability, the Examiner points out that the crystal form depends on the solvent used for formation of the crystals. Applicants do not disagree that the solvent is a parameter for achieving a particular crystalline form. Accordingly, the claims recite specific groups of solvent and the specification demonstrates examples of each group of solvents. It is thus predictable that the other solvents within each of the groups would act similarly.

As to the factor of amount of direction of working examples and the quantity of experimentation needed to make or use the invention, each group of solvents recited are described in the specification and working example of each group are provided. In *Invitrogen Vs Clontech,* 429 F.3d 1052 (Fed. Cir. 2005) (copy enclosed), the claims-in-suit were drawn to a genetically engineered RNase H deficient reverse transcriptase (RT), without regard for the method used to mutate the RT gene.

*Invitrogen*, 26 – 27. By the priority date at issue, 1988, the skilled artisan knew many techniques for altering genetic sequences, including deletion and point mutations. *Id.* The written description for the patents-in-suit described how to implement the claimed invention by deletion mutation; but it was disputed whether it also taught implementation via point mutation. *Id.* Clontech made at least one accused product by point mutation rather than deletion mutation. *Id.* And in its defense, Clontech argued Invitrogen's written description failed to enable claims encompassing point-mutated RT. *Id.* Since the claims did not exclude point-mutated RT, Clontech concluded that the claims must be invalid for lack of enablement. Id. The Court, however, rejected Clonetech's lack of enablement position:

> [Clonetech's] argument mistakes the purpose of the enablement requirement. Section 112 requires that the patent specification enable "those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation'" in order to extract meaningful disclosure of the invention and, by this disclosure, advance the technical arts.[16] Koito Mfg., 381 F.3d at 1155 (quoting Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (citation omitted)). Because such a disclosure simultaneously puts those skilled in the art on notice of the enforceable boundary of the commercial patent right, the law further makes the enabling disclosure operational as a limitation on claim validity. "The scope of [patent] claims must be less than or equal to the scope of the enablement. The scope of enablement, in turn, is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation." Nat'l Recovery, 166 F.3d at 1196; see also In re Goodman, 11 F.3d 1046, 1050 (Fed. Cir. 1993).
> ...

> Although Clontech's validity argument might have force had Invitrogen limited its claims to modified RT by reference to point mutation, Clontech overlooks the fact that the claims are not limited by the method of achieving the mutation. As the district court noted, **"[t]he enablement requirement is met if the description enables any mode of making and using the invention."** Johns Hopkins Univ. v. Cellpro, Inc., 152 F.3d 1342, 1361 (Fed. Cir. 1998); accord Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1335 (Fed. Cir. 2003); Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1533 (Fed. Cir. 1991). In this case Invitrogen's teaching regarding deletion mutation is sufficient to satisfy its part of the patent bargain, as it fully teaches a mode of making the claimed invention. **Enablement does not require the inventor to foresee every means of implementing an invention at pains of losing his patent franchise. Were it otherwise, claimed inventions would not include improved modes of practicing those inventions.**

*Invitrogen*, 26 – 29, bold emphasis added. Based on *Invitrogen*, it is clear that the Applicant's disclosure of one example of each group of solvent meets the enablement requirement as required by Section 112.

In *Johnshopkins Univ. Vs. Cellpro, Inc.* 152 F.3d 1342, 1361 (Fed. Cir. 1998) (copy enclosed and citations herein are to the enclosed copy page numbers), the Court again explained that enablement is not measured based on how many different ways the claims are enabled:

> CellPro argues that the claims of the '204 patent, which both parties agree are drawn to the genus of antibodies which bind to the claimed antigen, are not enabled as required by 35 U.S.C. § 112, 1, and that the district court erred in granting summary judgment to the contrary. CellPro contends that the patent discloses only the method of producing the anti-My-10 antibody and is therefore insufficient to

> enable one of ordinary skill in the art to make and use the broader genus of claimed antibodies.
> ...
> CellPro also cites the expert declaration of Dr. John Wijdenes in an attempt to prove that the amount of experimentation needed to successfully practice the invention disclosed in the '204 patent was undue.

*Johnshopkins*, 13 – 14. In constrast, the court held:

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.
>
> CellPro finally contends that no one ever succeeded in making CD34 antibodies using either purified My-10+ cells or immuno-precipitated My-10 antigens as the immunogens in the Kohler/Milstein method. See Hopkins I, 931 F. Supp. at 323. Hopkins argues that this fact, even if true, is legally irrelevant because the use of these immunogens was disclosed in the patent specification as alternatives to the preferred use of the KG-1/KG-1a cell line. See '240 patent, col. 5, l. 65 to col. 6, l. 27. Hopkins is correct; CellPro can carry its burden only by showing that all of the disclosed alternative modes are insufficient to enable the claims, because "[t]he enablement requirement is met if the description enables any mode of making and using the invention.

*Johnshopkins*, 15, underlining emphasis added. As held in *Johnshopkins*, the enablement requirement does not require that all the alternatives be described. Instead, in this application **any mode** of making and using the invention described with respect to specific solvents is sufficient. As in *Invitrogen* and *Johnshopkins*, all

the alternative solvents are described and demonstrated with respect to a representative of each group and the enablement requirement is met.

With respect to the more stringent written description requirement, *Amgen Inc. Vs Hoechst Marrion Roussel Inc.* (copy enclosed) stated:

> the purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required to "recount his invention in such detail that his future claims can be determined to be encompassed within his original creation." Id. at 1561, 19 USPQ2d at 1115 (citation omitted). Satisfaction of this requirement is measured by the understanding of the ordinarily skilled artisan." *Amgen*, 19.
> ...
> In addressing [the challenger's] written description arguments, the district court carefully examined whether Amgen's specification adequately described the full breadth of the claims. ... Acknowledging the presence of "a genuine dispute between the expert witnesses," the court weighed the testimony and found that the evidence showed that the descriptions adequately described to those of ordinary skill in the art in 1984 the use of the broad class of available mammalian and vertebrate cells to produce the claimed high levels of human EPO in culture. Amgen, 126 F. Supp. 2d at 149, 57 USPQ2d at 1507. In so doing, the court credited in particular the testimony of Amgen's expert, Dr. Harvey Lodish, who testified, among other things, that there might be "minor differences" in applying the method of the disclosed examples (utilizing CHO and COS-1 (monkey) cells) to any vertebrate or mammalian cells, but that those of ordinary skill could "easily" figure out those differences in methodology. Id., 57 USPQ2d at 1507.

*Amgen*, 19 – 20. As stated above, description relating only CHO and COS monkey cells is sufficient to support claims directed to all mammalian and vertebrate cells. Accordingly, a representative of the broad class has been taken to demonstrate the activity in the whole class as claimed. In the same line, the present application

provides sufficient description of each class of solvent claimed. Hence, such claims are allowable in light of the above case law. Turning to the more lenient enablement requirement, the district court noted:

> When the claim is to a composition rather than a process, the written description requirement does not demand that the specification describe technological developments in the way in which the claimed composition is made that may arise after the patent application is filed.

*Amgen*, 21. Further:

> the enablement requirement is often more indulgent than the written description requirement. The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation.

*Amgen*, 26. And:

> Focusing specifically on the '422 patent, the enablement inquiry is whether Amgen has enabled all pharmaceutical compositions comprising "a therapeutically effective amount of human erythropoietin," "a pharmaceutically acceptable diluent, adjuvant or carrier," and human erythropoietin "purified from mammalian cells grown in culture." The court found that the specification described and enabled various possible diluents and carriers and provided specific information on effective dosages and therapeutic effect in mice. ... Amgen also described and enabled at least one way of obtaining EPO purified from mammalian cells in culture: the genetic manipulation of CHO and COS-1 cells, followed by both described and other well known purification techniques. Finally, the court accepted testimony indicating that an ordinarily skilled artisan would infer from the COS-1 (monkey) and CHO cell examples that similar outcomes could be expected from other mammalian cells since all mammalian cells

> produce and secrete hormones like EPO by means of the same fundamental processes.

*Amgen*, 28. The disclosure at issue in Amgen provided a general description of an available adjuvant which could be used with the pharmaceutical composition along with the active erythropoietin. There were no specific examples for each and every adjuvant mentioned in the specification and yet the patent was not invalidated. Further even though only COS and CHO cells were described, it was held that similar outcomes would be achievable with other mammalian cells. Accordingly, the court acknowledges that enablement across the whole scope of genus claims may be demonstrated by a single representative for the genus.

Turning to the other patent at issue in Amgen, the Court stated:

> having disclosed one way to make the claimed EPO-producing cell, is Amgen entitled to claim all such cells that "can be propagated in vitro," comprise "non-human DNA sequences that control transcription," transcribe "DNA encoding human erythropoietin," and produce the claimed amount of EPO? While our precedent does hold that disclosure of one or two species may not enable a broad genus, e.g., In re Vaeck, 947 F.2d at 495-96, 20 USPQ2d at 1444-45, the district court made several fact-findings indicating that any gaps between the disclosures and the claim breadth could be easily bridged. See, e.g., Amgen, 126 F. Supp. 2d at 149, 57 USPQ2d at 1514 (crediting Amgen's expert Dr. Lodish's statement that "one of ordinary skill in the art, me, my students, would have understood this not to be limited to the specific types of cells that were used in this example, that other vertebrate cells, mammalian cells, could have been used")... .

Amgen, 29, underlining emphasis added. Based on the same reasoning, it would be expected that the skilled artisan would easily be able to work the present invention

with any individual solvent through the teaching of a representative of each solvent group in the specification.

Based on the cases above, it is clear that disclosing any mode of making and using the invention is enough to meet the enablement requirement. Moreover, undue experimentation does not refer to the quantity of experimentation if it is routine work. In the present application, examples describe a representative of each group of solvents and extending the teaching to other members of each group would merely be routine work. This routine work cannot be regarded as "undue experimentation" in view of both the specification and the above case law. In *Invitrogen*, a broad genus of mutation was claimed but only one type of mutation was described. But the claim was enabled, its scope extended to other mutations, and the defendant infringed the claim. Similarly, in the present application different groups of solvents are mentioned and one type of each group is demonstrated. Accordingly, claims reciting such a group or genus is enabled in light of the above case law. Also, the case laws points out that a representative of a whole genus enables a genus since the members of the genus are known and likely to work in the same manner. Specifically, in *Amgen*, limited description of adjuvants in the specification enabled claims reciting adjuvants not listed. Accordingly, Applicants respectfully submit that demonstration of one representative of each group of solvents meets the enablement requirement.

Claims 2 - 3 depend from claim 1 and are similarly enabled. Based on the foregoing, Applicants submit that claims 1 – 3 are enabled and the rejection is improper. Applicants respectfully request withdrawal of the 35 U.S.C. §112, first paragraph enablement rejection of claims 1 – 3.

***Claim Rejections - 35 USC §112, second paragraph.***

The Examiner rejects claims 1 and 2 as indefinite under 35 U.S.C. §112, second paragraph. Corrective amendments obviate the rejections and Applicants respectfully request the withdrawal of each rejection under 35 U.S.C. §112, second paragraph.

***Conclusion***

If the Examiner believes that any additional matters need to be addressed in order to place this application in condition for allowance, or that a telephone interview will help to materially advance the prosecution of this application, the Examiner is invited to contact the undersigned by telephone at the Examiner's convenience.

In view of the foregoing amendment and remarks, Applicants respectfully submit that the present application, including claims 1 – 3, is in condition for allowance and a notice to that effect is respectfully requested.

Respectfully submitted,

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